REMARKS

The Office Action of August 26, 2004 raises numerous objections to the specification and claims and rejected all of the pending claims except for claim 28, which was identified as being allowable. Reconsideration of the objections and rejections raised in the Office Action are respectfully solicited in view of the following remarks and in light of the provided amendments.

Amendments to the Specification

The specification is amended to make appropriate reference to trademarked products, add generic terminology describing the trademarked products, and to correct an obvious typographical error that is identified in the Office Action of August 26, 2004. It is noted that complete capitalization of the trademarked terms is not employed in the amendments as the trademark owners use differential capitalization when describing these products. No new matter is added by way of these amendments.

Amendments to the Claims

Claims 1, 2, and 37 are hereby cancelled, without prejudice or disclaimer. Claims 3 and 4 are amended so as to make claims 3-15 dependent on independent claim 16. This reflects the fact that claim 16 is directed to production of proteins generally by way of transfecting a cell with a nucleic acid molecule comprising a S/MAR element selected from SEQ ID NOs:1-5, a highly identical sequence thereto, or a functional fragment thereto and that amended claim 3 and claims 4-15 are directed to the production of specific proteins, Factor VII and Factor VII-related polypeptides, by practice of such a method.

The claim amendments find support in the originally-filed specification and claims. Accordingly, no new matter has been added by these amendments.

Claims 3-36 and 38-41 are pending. Claims 16, 28, 37, 39, and 41 are the only independent claims.

The Inventor Declaration

The Office Action objected to the Declaration filed January 20, 2004, in that the Declaration includes an alteration that is not initialed. Applicants submit herewith a newly executed inventor Declaration so as to address the objection raised in the Office Action with respect to the Declaration filed on January 20.

The Objections and Informalities Have Been Addressed

The Office Action objected to the improper use of trademarked terms in the specification and to a typographical error in the specification. The Office Action further objected to the use of the abbreviation S/MAR in the claims without first spelling out the term and indicating the meaning of the abbreviation therein. Applicants wish to thank Examiner Desai for his careful review of the application.

The amendments to the specification and claims provided here are believed to address all of the formality rejections raised in the Office Action. Trademarked terms are acknowledged in the amended specification, typographical errors are corrected, and appropriate use of the abbreviation "S/MAR" is made in the amended claims. Accordingly, all of the informalities and objections in the Office Action are believed to be addressed by the present amendments.

The Pending Claims Are Sufficiently Definite

The Office Action rejected claims 3, 4, 15, 16-27, and 30-41 under 35 USC § 112, 2nd ¶, as allegedly being indefinite. Applicants respectfully submit that these rejections are either misplaced or addressed by the present amendments.

The Office Action alleged that the use of the phrase "70% homologous" in claims 3 and 16 was indefinite. The term "homology" is substituted (as suggested by Examiner Desai) in the amended claims by the term "identity". Accordingly, this alleged indefiniteness is addressed by the claim amendments.

The Office Action further alleged that the phrase "expression control elements" used in claims 36 and 39 was indefinite. In this respect, the Office Action

asked: "What is meant by 'expression control elements'? Would a S/MAR be an 'expression control element?'"

The test for definiteness under 35 U.S.C. 112, 2nd ¶, is whether "those skilled in the art would understand what is claimed when the claim is read in light of the specification." See, e.g., MPEP § 2173.02 and *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576 (Fed. Cir. 1986).

Applicants respectfully submit that the phrase "expression control element" would be understood by one of ordinary skill in the art when read in view of the present specification. Description of "expression control elements" can be found at, e.g., paragraph 0041 of the published application (i.e., US Patent Application Pub. No. 2004-0115776). The specification indicates the phrase refers to "regulatory elements such as transcriptional promoters, enhancers, RNA polymerase binding sites, polyadenylation sites, translation initiation signals, and termination signals"). Thus, one of ordinary skill in the art, particularly given this description, would have a reasonable understanding of what the claim element encompasses. Moreover, given this description and the distinct usage of this phrase from "S/MAR element" in the claims and specification, the ordinarily skilled artisan would understand that the phrase does not refer to additional S/MAR elements. Applicants further note that the phrase "expression control elements" is *routinely* used in issued US patent claims (see, e.g., recently issued US Patents 6,686,188; 6,656,700; 6,815,575; 6,720,309; 6,627,617; 6,326,166; and 6,291,240), evidencing the fact that artisans would sufficiently understand the meaning of this claim element. In view of these facts, Applicants respectfully submit that this indefiniteness rejection is misplaced.

The Office Action additionally alleged that the phrase "consisting essentially of" in claim 41 is indefinite. This rejection also appears misplaced, particularly in view of the well-established legal meaning assigned to this transitional phrase in US patent practice (see, e.g., MPEP § 2111.03). Accordingly, Applicants request that the rejection be withdrawn. Applicants note that "if the language used by applicant satisfies the statutory requirements of 35 U.S.C. 112, second paragraph, but the

examiner merely wants the applicant to improve the clarity or precision of the language used, the claim must not be rejected under 35 U.S.C. 112, second paragraph." The Examiner's suggested amendment is appreciated, but not adopted, and is not necessary to satisfy the definiteness requirement.

The Office Action also alleged that the use of the phrases "at least about" in claims 3, 4, and 16 and "less than about" in claims 15 and 30 rendered these claims indefinite. Applicants respectfully disagree. Applicants note that the use of the relative term "about" is generally considered acceptable claim language, particularly where the ordinarily skilled artisan would generally understand what is covered by the claim and/or there is some guidance in the specification as to how the term would be understood, provided that there are no issues of close prior art at hand (see, e.g., MPEP § 2173.05(b)). With respect to amended claim 16, specifically, the phrase "at least about 70% identical" would be reasonable understood by one of ordinary skill in the art given the relevant teachings of the specification (see, e.g., paragraphs 0011 and 0012) and the common usage of such relative language in defining similar nucleotide sequences to a reference sequence (see, e.g., US Patents 6,299,869; 6,177,611; 6,130,316; 6,103,511; 6,096,305; 6,027,915; 6,500,942; 6,566,511; 6,271,349; 6,242,566; 6,391,847; 6,806,061; and 6,608,240). In this respect, Applicants note that the "standards of patentability applied in the examination of claims must be the same throughout the Office." MPEP § 706. Given the regular use of such claim language in similar context in so many recently issued US patents, this indefiniteness rejection appears clearly misplaced and, accordingly, withdrawal is respectfully solicited. For similar reasons, reconsideration of the rejection of claims 15 and 30 as indefinite for use of the phrase "less than about 10 kb" is respectfully requested (see, e.g., paragraph 0041, providing guidance as to the meaning of the phrase, and US Patents 6,492,115; 6,458,536; 6,566,128; 5,508,468; and 5,360,715, evidencing the frequent use of such relative language with respect to lengths of nucleic acid sequence claim elements).

The remaining indefiniteness rejections were based solely on dependence on a rejected claim. Accordingly, all of the indefiniteness rejections raised in the Office Action are believed to be hereby addressed, and are either overcome by the present amendments or initially misplaced.

The Claims Meet the Written Description Requirement

The Office Action rejected claims 1-27 and 29-40 for allegedly failing to comply with the written description requirement of Section 112, 1st ¶. Reconsideration is respectfully solicited.

Specifically, the Office Action alleged that because the specification supposedly does not teach a "functional fragment" of a S/MAR or a "functional analogue" of a human protein that claims 3, 4, 16, and 29 do not comply with the written description requirement. The Office Action cited the Federal Circuit's 1997 decision in *University of California v. Eli Lilly and Co.* in support of this rejection.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., MPEP 2163; *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319 (Fed. Cir. 2003). Satisfaction of the written description requirement is measured by the understanding of the ordinarily skilled artisan. See, e.g., *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1330 (Fed. Cir. 2003). The Federal Circuit in *Amgen* clearly articulated the relevance of its earlier holding in *Eli Lilly*: "[I]n *Enzo Biochem* [Fed. Cir. 2002], we clarified that *Eli Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure. See Enzo Biochem, 296 F.3d at 1324, 63 USPQ2d at 1613." *Id.* at 1332.

Here, functional analogues of the S/MAR elements of the claims are sufficiently descried with respect to the written description requirement by reference to specific

nucleotide sequences (i.e., SEQ ID NOs:1-5). Accordingly, the "disclosed function" (i.e., exhibiting S/MAR activity similar to one of SEQ ID NOs:1-5) is sufficiently correlated to a "disclosed structure" (i.e., having a sequence similar to or being a substantial portion of one of SEQ ID NOs:1-5). Similar usage of the phrase "functional fragment" in the context of nucleotide sequences is widely accepted in the art (see, e.g., US Patents 6,706,493 (claim 1); 6,794,170 (claim 1); 6,767,720 (claims 6 and 7); 6,576,422 (claim 7); 6,566,110 (claim 1); 6,541,244 (claim 3); 6,287,795 (claim 1); 6,365,394 (claim 15); 6,475,775 (claim 5); 6,485,966 (claim 16); 6,534,476 (claim 3); 6,670,114 (e.g., claim 1); 6,590,079 (e.g., claim 9)). Accordingly, Applicants submit that the written description rejection is misplaced and should be withdrawn.

One of Ordinary Skill is Enabled to Practice the Claimed Invention

The Office Action rejected claims 1-27 under the enablement requirement of Section 112, 1st ¶. Specifically, the Office Action stated that the specification, "while being enabling for producing Factor VII by transfecting a mammalian cell with a nucleic acid molecule comprising a scaffold/matrix attachment region identified by SEQ ID NO:1-5, [the application] does not reasonably provide enablement for producing Factor VII by transfecting a mammalian cell with a nucleic acid molecule comprising any scaffold/matrix attachment region." Applicants note that the present claim amendments limit the claims to S/MAR elements comprising one of SEQ ID NOs:1-5, sequences that are highly identical to one or more of SEQ ID NOs:1-5, and functional fragments of SEQ ID NOs:1-5. Thus, the amended claims do not involve "any scaffold/matrix attachment region."

An ordinarily skilled artisan would be able to put the full scope of this claimed invention into practice with no more than routine experimentation. Production of various recombinant cells; identification and generation of highly similar nucleic acid sequences to a disclosed reference sequence; and generation of functional fragments of specific sequences are all within the repertoire of one of one of ordinary skill in the art.

The published literature is replete with examples of such methodologies being performed with numerous types of nucleic acid sequence elements.

Applicants also note that the Office Action appears to apply an incorrect standard for entering these enablement rejections. Specifically, the Office Action refers to "not invariably" resulting in expression of any polypeptide with any S/MAR element and the predictability of the results "not [being] invariable." Invariability is certainly not required for satisfying the enablement requirement (see, e.g., *In re Wands,* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), noting that a success rate of less than 50% was acceptable and suggesting that even a success rate of less than 3% would be sufficient if the amount of experimentation required for success was routine).

In view of the present amendments and above-mentioned recent Federal Circuit guidance, the pending claims are believed to meet the enablement requirement. Reconsideration is accordingly respectfully solicited.

The Pending Claims Are Not Anticipated by the Cited Art

The Office Action rejected claims 16-18 under 35 USC § 102(b) as allegedly anticipated by US Patent 5,888,774 to Decuve. This rejection is overcome by the present claim amendments.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

The Decuve '774 patent does not teach, or even suggest, a S/MAR element comprising one of SEQ ID NOs:1-5, a sequence that has at least about 70% identity to one of such sequences, or a functional fragment of such sequences. Accordingly, none of the amended claims are anticipated by the Decuve '774 patent.

Prima Facie Obviousness Has Not Been Established For Any Pending Claim

The Office Action rejected claims 1-5, 15-18, and 36 under 35 USC § 103(a) as allegedly encompassing obvious subject matter over the Decuve '774 patent in view of US Patent 4,784,950 (Hagen et al.).

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. See, e.g., In re Royka, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974).

As noted above, there is no teaching or suggestion in the Decuve '774 patent of a S/MAR element comprising a sequence according to one of SEQ ID NOs:1-5, a functional fragment of one of such sequences, or a sequence that has at least about 70% identity to one of such sequences. Accordingly, the pending claims appear free of the cited art.

Conclusion

It is respectfully submitted that the application and claims are in good and proper form for allowance. Early action to that end is respectfully submitted. The Commissioner is hereby authorized to charge any fees in connection with this application and to credit any overpayments to Deposit Account No. 14-1447. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, or there are any questions remaining concerning the application or this amendment, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

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